First-in-human, phase 1a, dose escalation study of BGB-B167, a CEA x 4-1BB bispecific antibody, as monotherapy or combined with tislelizumab (anti-PD-1), in patients with selected advanced or metastatic solid tumors

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ABSTRACT

Background: BGB-B167 is potentially a first-in-class IgG-based bispecific antibody that targets CEA, a tumor-associated antigen overexpressed in many cancers, and 4-1BB, a key T-cell co-stimulatory receptor expressed on activated CD4+/CD8+ T lymphocytes. Preclinical data suggest BGB-B167 binds to these target proteins with high specificity/affinity, inducing T-cell activation and antitumor activity, with potential for mitigating strong AEs, eg CRS and hepatoxicity. We present results of a first-in-human, phase 1a, open-label, multicenter trial of BGB-B167 given as monotherapy (Part A [A]) or with tislelizumab (TIS) (Part B [B]) (NCT05494762).

Methods: Eligibility: ≥18 y with unresectable/metastatic CRC, CEA+ GC or CEA+ NSCLC previously treated with standard systemic therapy or for whom treatment is unavailable; pts with CRC and known MSI-H/dMMR status must have received prior ICI, if available. Primary objectives: safety/tolerability; MTD and RP2D for BGB-B167 ± TIS; key secondary objective: antitumor activity (RECIST v1.1).

Results: As of July 7, 2024, 54 pts were enrolled (31 in A, 23 in B) with BGB-B167 dose ranges of 5–1200 mg IV QW assessed in A and 50–600 mg IV QW in B. In A and B, respectively, 29/31 (93.5%) and 18/23 (78.3%) had CRC, 2/31 (6.5%) and 3/23 (13 GC, 0/31 (0%) and 2/23 (8.7%) had NSCLC; 19/31 (61.3%) and 18/23 (78.3%) had liver metastases; 20/31 (64.5%) and 14/23 (60.9%) received ≥3 lines of prior therapy. TEAEs occurred in all pts (**Table**). Most common treatment-related TEAEs were nausea (4/31; 12.9%) and fatigue (3/31; 9.7%) in A and pruritus (5/23; 21.7%) and diarrhea (4/23; 17.4%) in B; there were no treatment-related TEAEs indicative of hepatotoxicity or CRS. There was a single DLT (gr 3 SJS) in a pt who received 600 mg BGB-B167 + TIS (resolved after treatment discontinuation). MTD was not reached. 3 pts (1 with CRC [A]; 1 with CRC and 1 with GC [B]) had confirmed PRs. DoR was ≥5.6 mo for the pt in A and ≥5.6 mo and ≥6.9 mo for the pts in B; all remained on treatment with ongoing responses as of the data cutoff date. DCR (95% CI) was 33.3% (17.3–52.8) in A and 40.9% (20.7–63.6) in B. Serum exposure of BGB-B167 increased dose dependently from 150 to 1200 mg.

Conclusion: Overall, BGB-B167 ± TIS was well tolerated and has demonstrated limited antitumor activity in pts with advanced/metastatic CEA+ solid tumors.

Safety

	Part A BGB-B167 monotherapy (N=31)	Part B BGB-B167 + TIS (N=23)
Any TEAE	31 (100.0)	23 (100.0)
Any treatment-related TEAE	17 (54.8)	15 (65.2)
Gr ≥3	4 (12.9)	1 (4.3)
Serious	0 (0)	2 (8.7)
Leading to death	0 (0)	0 (0)
Leading to treatment discontinuation	0 (0)	1 (4.3)
Any imAE	2 (6.5)	5 (21.7)
IRRs	4 (12.9)	6 (26.1)

Patients with multiple adverse events (AEs) are counted once. All AEs are listed as n (%). imAE, immune-mediated AE; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.